ABSTRACTS

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Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarction, and death: The vitamin intervention for stroke prevention (VISP) randomized controlled trial

Toole JF, Malinow MR, Chambless LE, et al. JAMA 2004; 291:565-75.

Conclusion: Vitamin therapy resulting in moderate reductions of total homocysteine after a nondisabling cerebral event has no affect on vascular outcomes during a 2-year follow up period.

Summary: The authors sought to determine if high doses of folic acid, pyridoxine (vitamin B_6), and cobamalin (vitamin B_{12}) could lower the risk of death, recurrent cerebral infarction, and coronary heart disease in patients with a nondisabling cerebral infarction. A total of 3680 adults with nondisabling cerebral infarction were randomized at 56 centers to receive best medical and surgical care plus a daily vitamin containing either high-dose formulations of pyridoxine (25 mg), cobamalin (0.4 mg), and folic acid (2.5 mg) or a low-dose formulations containing 200 μg of pyridoxine, 6 μg of cobamalin, and 20 μg of folic acid.

There was a graded and persistent association between baseline total homocysteine level and outcome. Risk association with baseline homocysteine level was numerically slightly lower in the high-dose group for all events but was not statistically different from that in the low-dose group. Mean total homocysteine levels were reduced to a greater extent in the high-dose group than in the low-dose group (2 μmol/L). There were no differences in the high-dose or low-dose groups with respect to recurrent cerebral infarction, coronary heart disease, or death. There was an 18% chance of an event within 2 years in the high-dose vitamin group and an 18.6% chance of an event within 2 years in the low-dose vitamin group. The risk of ischemic stroke within 2 years was 9.2% for the high-dose and 8.8% for the low-dose group ($P = .80$).

Comment: The lack of treatment effect of vitamin therapy on cardiovascular end points observed in this study may be due to several factors. Homocysteine levels in the study population were relatively low and treatment effects may be more pronounced in patients with higher levels of homocysteine. Alternatively, US government–mandated folic acid supplementation of the grain supply may have mitigated additional vitamin effects. A longer period of observation may also be necessary to observe treatment effect.

Endovascular treatment of isolated atherosclerotic stenosis of the infrarenal abdominal aorta: Long-term outcome

Feugier P, Toursarkissian B, Chevalier J-M, et al. Ann Vasc Surg 2003;17: 375-85.

Conclusion: Aortic angioplasty is an effective treatment for isolated atherosclerotic stenosis of the infrarenal abdominal aorta, with primary patency rates of 94% at 1 year, 89% at 3 years, and 77% at 5 years.

Summary: A total of 86 patients (36 women, 50 men, mean age 53.2 ± 12.7 years) from 18 European centers who underwent endovascular treatment of symptomatic atherosclerotic occlusive lesions of the infrarenal abdominal aorta were evaluated. Only cases of isolated stenosis confined to the infrarenal aorta >10 mm from the aortic bifurcation were included. Indication for treatment was claudication in 74 of the 86 cases. Mean preprocedure ankle-brachial index was 0.71 and mean diameter reduction of the aorta was 77%. There was circumferential aortic calcification in 35%. A single balloon technique was used in 60 cases and a double balloon technique in 26 cases. Stents were employed in 88% of cases.

There was one mortality unrelated to treatment of the aortic lesion. There were four technical failures with residual stenosis >30%. Early morbidity occurred in 9.3% and included retroperitoneal hematoma in one patient, peripheral embolism in two patients, and puncture site hematoma in three patients. Survival at 3 years was 91%. Primary patency of the angioplasty sight was 94% at 1 year, 89% at 3 years, and 77% at 5 years. Three patients developed aortic thrombosis at the treatment site at 8, 41, and 49 months, respectively. Sixty-five patients (76%) were symptomless at last follow-up. The mean ankle-brachial index at follow-up was 0.89 ($P < .01$ compared with pretreatment values). Age, gender, length of stenosis, circumferential aortic calcification, and stent usage did not affect long-term patency.

Comment: This article has all of the disadvantages of a retrospective study, including varying techniques of angioplasty, different stents, lack of consistent use of pressure gradients, and no consistent follow-up protocol. Nevertheless, very acceptable initial technical success and reasonable long-term primary patency appear possible with aortic dilatation.

$P2Y_{12}$ H2 haplotype is associated with peripheral arterial disease: A case controlled study

Fontana P, Gaussen P, Haiach M, et al. Circulation 2003;108:2971-2973.

Conclusion: The H2 haplotype of the platelet ADP receptor $P2Y_{12}$ may be important in the development of atherosclerotic peripheral arterial disease (PAD) independent of diabetes, smoking, hypertension, and hypercholesterolemia.

Summary: After platelet adhesion to endothelium, platelet aggregation participates in development of atherosclerosis through release of growth factors and cytokines. The $P2Y_{12}$ receptor for ADP is particularly important in mediating platelet aggregation in patients with PAD. Specific blockage of this receptor by clopidogrel provides benefit against ischemic events in patients with PAD compared with those with histories of myocardial infarction and stroke with no known PAD (Lancet 1996:348;1329-1339). There are two haplotypes of the $P2Y_{12}$, H1 and H2, with H2 leading to greater ADP-induced platelet aggregation. The authors tested the link between the H2 haplotype of $P2Y_{12}$ and PAD in a case controlled study.

Male patients <70 years of age with PAD (n = 184) were compared with 330 age-matched controls free of symptomatic PAD. In univariant analysis the H2 haplotype was more frequent in patients with PAD than in control subjects (30% and 21%, respectively; odds ratio 1.6; confidence interval 1.1-2.5; $P = .02$). In multivariable analysis this association remained significant after adjustment for diabetes, smoking, hypertension, hypercholesterolemia, and other platelet receptor gene polymorphisms (odds ratio 2.3; confidence interval 1.4-3.9; $P = .002$).

Comment: The data indicate a possible role for a specific gene polymorphism in the development of PAD. Genetic testing may some day be employed to determine which antiplatelet agent is likely to have the greatest protective effect in an individual patient with PAD.

Mechanism of ischemic infarct in spontaneous carotid dissection

Benninger DH, Georgiadias D, Kremer C, et al. Stroke 2004;35:482-5.

Conclusion: Thromboembolism, not hemodynamic infarction, is the primary stroke mechanism in patients with spontaneous carotid dissection.

Summary: The authors retrospectively evaluated brain computed tomography (CT) and magnetic resonance (MR) scans and ultrasound findings of 141 consecutive patients with 143 spontaneous carotid dissections causing ischemic stroke. Eleven patients were excluded because of technical considerations or treatment with thrombolysis. Overall, data from 130 patients with 131 spontaneous carotid dissections were analyzed.

There were 76 men and 54 women in the study, mean age 45 ± 11 years. Carotid artery dissections were unilateral in 123 cases (94%). Three patients had asymptomatic dissection of the opposite internal carotid artery, and three patients had asymptomatic dissection of a vertebral artery. Ischemic strokes were studied by MR imaging and CT in 72% of patients, MR imaging alone in 8% of patients, and CT alone in 20% of patients. Territorial infarcts, indicative of thromboembolic disease, were found in all patients. Additional border zone infarcts, indicating hemodynamic infarction, were seen in six patients. Territorial infarcts affected the middle cerebral artery in 130 of the 131 cases. Patterns of cross flow, degree of internal carotid artery stenosis, number of middle cerebral and anterior cerebral artery occlusions, and middle cerebral artery stenoses did not differ between carotid artery dissections causing territorial and border zone infarcts and those dissections only resulting in territorial infarcts. Recurrent ischemic events were observed in three patients during the first 2 weeks. All were transient ischemic attacks.

Comment: The overwhelming mechanism for ischemic infarct in patients with spontaneous carotid dissection is thromboembolism. A thromboembolic mechanism of ischemic infarction in spontaneous carotid dissection likely explains the well-recognized therapeutic benefit of anticoagulation for treatment of spontaneous carotid dissection.

Peripheral arterial disease in people with diabetes: American Diabetes Association Consensus Statement

Diabetes Care 2003; 26:3333-41.

Summary/Conclusions: This article grew out of a consensus conference held May 7-8, 2003, under the hospices of the American Diabetes Association. Four topics were addressed: (1) the epidemiology and impact of